would have been obvious. All of the broadly claimed substances are known to inhibit antibiotics.

The only compound described by Langeveld to reduce test sensitivity is cysteine. Langeveld describes the use of cysteine to reduce test sensitivity to the penicillins. Even if we assume arguendo that cysteine will work to reduce sensitivity to penicillins, both Langeveld, and relevant literature (Exhibits 2 & 3) indicate that cysteine will not similarly reduce test sensitivity to the cephalosporin group of beta-lactams. That is, cysteine does not reduce test sensitivity to the whole beta-lactam family, only the penicillin group. This distinction is important for tests that require sensitivity adjustment for the whole beta-lactam family. This distinction is particularly important in tests that are overly sensitive to the cephalosporins, as compared to other beta-lactam antibiotics, to be detected. In such tests, cysteine would work contrary to the desired result.

Unlike cysteine, a microbial receptor that is extracted from a bacteria with sensitivity to all beta-lactams, can reduce test sensitivity to all beta-lactams. By reducing sensitivity to all beta-lactams, test sensitivity can be increased relative to other antibiotics, for example, through coarse sensitivity adjustment techniques such as adjusting pH, while maintaining or even reducing the beta-lactam sensitivity.

A goal in antibiotic detection is to produce tests that accommodate the industry accepted tolerance levels but that are not overly sensitive. (Exhibit 4, page 3 and Exhibit A - Declaration of Robert S. Salter). Overly sensitive tests can result in the disposal of food that is considered fit for human consumption (Exhibit 5, page 151). In Europe, the regulatory level (MRL level) for tetracycline is 100 ppb and the MRL level for cephapirin is 60 ppb. Broad spectrum microbial inhibition assays for deteting beta-lactams and other antibiotics, particularly those using *B.st.* as the culture organism, are sensitive to cephapirin well below 60 ppb, sensitive to the penicillins just below the MRL level, but relatively insensitive to tetracycline. It is valuable, therefore, to have the ability to make a coarse increase in test sensitivity, thereby increasing sensitivity to tetracycline, while adding a substance to offset the increase in sensitivity by decreasing, relative to

tetracycline, the test sensitivity to cephapirin and other beta-lactams. As testified to by Robert S. Salter (Exhibit A, paragraph 13), use of cysteine would be counterproductive relative to test sensitivity to the cephalosporins.

Applicant respectfully suggests that it is only in hindsight that it becomes obvious to selectively adjust sensitivity of the broad spectrum microbial inhibition assay by adding the microbial receptor with sensitivity to beta-lactams. Evidence of this is provided by the Declaration of Robert S. Salter (Exhibit A) in which Mr. Salter describes the long-felt, unresolved need in the art for such a sensitivity adjustment method.

Nothing in the art suggests the combination of a microbial receptor extracted from a beta-lactam sensitive bacteria with a microbial culture containing the same receptor, as a constituent component, in a microbial inhibition test to detect a broad range of antibiotics. Indeed, that such extracted receptors were long known and available but never used in this manner is evidence that such a combination was non-obvious. Further evidence of the non-obviousness of the combination, as testified to by Robert S. Salter in Exhibit A, paragraph 17, is the unpredictable nature of microbial inhibition test development.

Applicant has amended claim 1 to reflect that test sensitivity of a microbial inhibition test for detecting multiple antibiotic families, including beta-lactams, is adjusted using a microbial receptor, extracted from a bacteria, with sensitivity to beta-lactams.

Applicant believes that the Office's concerns have been addressed.

Withdrawal of the rejections of claims 3-5, 8, 13-17, 23, and 30-37 under 35 U.S.C. 103(a) and favorable consideration is respectfully requested based on the amendments and remarks above.

Rejection under 35 U.S.C. 112 (first paragraph)

Claims 1-13 and 23-37 were rejected under 35 U.S.C. 112, first paragraph, for the reason that the specification is enabling for only selected substances. Specifically, the Office Action explained "in claim 1, the terms 'a substance that reduces the culture growth inhibition of the antibiotic' lacks enablement." Applicant submits that the currently amended claim 1, and the claims depending from claim 1, as amended, addresses the Office's concern.

Applicant has amended independent claim 1 to specify that the substance used to adjust test sensitivity is a microbial receptor, extracted from a bacteria, with sensitivity to beta-lactams. The specification generally provides support for claim 1 as amended. For example, paragraph 0032 describes using beta-lactam receptors from various bacterial species.

Withdrawal of the 35 U.S.C. 112 (first paragraph) rejection and favorable consideration is respectfully requested based on the amendments and remarks above.

Rejection Under 35 U.S.C. 112 (second paragraph)

Claims 1-37 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office Action explained, "that there are many instances of lack of antecedent basis in the claims." Applicant thanks the Office for its recognition of the informality and has amended the claims to add antecedent basis. Applicant respectfully believes that this amendment addresses the Office's concerns and favorable reconsideration is respectfully requested.

Additionally, the Office has noted that claim 1 "reads on water" because claim 1 lacks selectivity of the substance that reduces the culture growth inhibition of the antibiotic. In response, Applicant has amended claim 1 to specify that the substance used to adjust test sensitivity is a microbial receptor. The specification generally provides

support for claim 1 as amended. For example, paragraph 0032 describes using beta-lactam receptors from various bacterial species.

CONCLUSION

Applicant believes that the above amendments and remarks are fully responsive to the Office Action, thereby placing this application in condition for allowance and such action is respectfully requested. Applicant respectfully notes that because Applicant has addressed certain comments of the Office does not mean that Applicant concedes other comments of the Office. Further, the fact that Applicant has made arguments for the patentability of some claims does not mean that there are not other good reasons for the patentability of those or other claims.

Applicant requests speedy reconsideration, and further requests that the Examiner contact its attorney if there are any remaining issues.

Please charge any outstanding fees or credit any overpayments to Deposit Account No. 50-3152, Ref. No. 0656-032US3A.

Respectfully submitted,

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